August 22, 2003

Donald A. Lederer
Product Stewardship Manager
Solutia Inc
PO Box 66760
St. Louis, MO 63166-6760

Dear Mr. Lederer:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for the Mononitroanilines Category posted on the ChemRTK HPV Challenge Program Web site on April 21, 2003. I commend Solutia, Inc. for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed Comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that Solutia, Inc. advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission. Please send any electronic revisions or comments to the following addresses: oppt.ncic@epa.gov and chem.rtk@epa.gov.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

Oscar Hernandez, Director
Risk Assessment Division

Enclosure

cc: C. Auer
R. Gonzalez
W. Penberthy
M. E. Weber

EPA Comments on Chemical RTK HPV Challenge Submission:
Mononitroanilines Category

Summary of EPA Comments

The sponsor, Solutia, Inc., submitted a test plan and robust summaries to EPA for mononitroanilines dated April 9, 2003. EPA posted the submission on the ChemRTK HPV Challenge Web site on April 21, 2003. The category consists of two sponsored compounds: 2-nitrobenzeneamine (ONA, CAS No. 88-74-4) and 4-nitrobenzeneamine (PNA, CAS No. 100-01-6).

EPA has reviewed this submission and has reached the following conclusions:

1. Category Justification. Overall, the physicochemical and environmental fate properties, as well as the health and ecological effects data, support the mononitroanilines category.

2. Physicochemical Properties. The data provided by the submitter for melting point, boiling point, octanol/water partition coefficient, and water solubility are adequate for the purposes of the HPV Challenge Program. The submitter needs to verify the vapor pressure value for PNA.

3. Environmental Fate. The data provided by the submitter for photodegradation, stability in water, and fugacity are adequate for the purposes of the HPV Challenge Program. The submitter needs to correct its conclusions for the biodegradation of PNA.

4. Health Effects. Available data for most health effects endpoints are adequate for the purposes of the HPV Challenge Program. EPA reserves judgement on the adequacy of the two-generation reproductive toxicity data for PNA, pending receipt of a revised robust summary specifying effect levels. In addition, the submitter needs to address other deficiencies in the robust summaries.

5. Ecological Effects. Available data for toxicity to fish and aquatic invertebrates are adequate for the purposes of the HPV Challenge Program. The submitter needs to provide a missing data element in one of the robust summaries. The submitted data for algae are inadequate.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

EPA Comments on the Mononitroanilines Challenge Submission

Category Definition

The proposed category comprises two anilines containing a nitro function ortho or para to the amine: 2-nitrobenzeneamine (o-nitroaniline, ONA; CAS No. 88-74-4) and 4-nitrobenzeneamine (p-nitroaniline, PNA; CAS No. 100-01-6). These compounds are intermediates in the production of other industrial chemicals, including dyes, pigments, polymers, and water-treatment chemicals. The submitter's category definition is clear and unambiguous.

Category Justification

The submitter bases the justification of the Mononitroanilines category on the structural similarities of the members and the demonstrated similarities in their physicochemical and environmental fate properties, as well as health and ecological effects.

EPA agrees with the submitter that the physicochemical and environmental fate properties of these two mononitroanilines are similar. Further, the two compounds elicit similar mammalian toxicologic and ecological effects. Consequently, the data provided by the submitter support the category.

Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility)

The data provided by the submitter for melting point, boiling point, octanol/water partition coefficient, and water solubility are adequate for the purposes of the HPV Challenge Program.

Vapor pressure. With regard to PNA, the Dixon and Rissman (1985) citation does not include the primary source for the cited values; therefore, they cannot be identified as either measured or calculated. Furthermore, the value provided by the submitter does not agree with a measured value for ONA found by EPA, 0.0000032 mm Hg (Ferro, D. and Piacente, V. Heat of vaporization of o-, m-, and p-nitroaniline. Thermochim Acta 90: 387-9 (1985)). The submitter needs to verify this value.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity)

The data provided by the submitter for photodegradation, stability in water, and fugacity are adequate for the purposes of the HPV Challenge Program.

Biodegradation. Although ready biodegradability tests are not available, in this case the data presented by the submitter are adequate for the purposes of the HPV Challenge Program. While the PNA SCAS test data suggest some biodegradability, the nature of the test, the results obtained, and certain observations in the course of the study suggest that PNA, like ONA, will resist biodegradation (the robust summary indicates that PNA appeared to be moderately degradable; that the data obtained were somewhat erratic; that during the last two months of testing, far lower rates were observed: and that substantial inhibition of the normal sludge growth rate occurred). EPA located data confirming that PNA is not significantly biodegradable: (1) 0% ThBOD in 14 days (OECD 302C; Ref. 1); (2) degradation in > 64 days (screening study with soil inoculum, aerobic; Ref.2).

The submitter incorrectly states that PNA is “readily biodegradable”. Ready biodegradability cannot be inferred from positive results in an inherent biodegradability test. The submitter needs to correct its conclusion.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity)

Data submitted for both mononitroanilines as regards acute toxicity, repeated-dose toxicity, genetic toxicity, and developmental toxicity endpoints were adequate for the purposes of the HPV Challenge Program. The adequacy of a reproductive toxicity assay on PNA cannot be determined from the data provided; however, relevant data from the repeated-dose assay would be acceptable. The submitter’s read-across approach to reproductive toxicity for ONA is reasonable. The submitter needs to address deficiencies in the robust summaries.

Repeated-dose toxicity. The test plan misstated the results for systemic toxicity of ONA (text section 2.0, third paragraph, line 11-12). Hematological changes were significant in both sexes, as correctly noted in lines 14-16 in the same paragraph.

Reproductive toxicity. No data were submitted for ONA. The adequacy of a two-generation study on PNA cannot be determined because of the lack of an effective dose. The highest dose tested, 9 mg/kg/day, was the NOAEL. The submitter can nonetheless satisfy the reproductive toxicity endpoint by describing in robust summary format the reproductive histopathology from the PNA 90-day repeated-dose assay results. The submitter’s plan to use a read-across approach for this endpoint is justified on the basis of generally similar toxic effects of ONA compared to PNA.

Developmental toxicity. The submitter needs to provide more information on maternal toxicity in the ONA study so that the discrepancy in the NOAELs among the test plan (Table 9), robust summary, and repeated-dose assays can be addressed.

Ecological Effects (fish, invertebrates, and algae)

Adequate data from two fish and two invertebrate toxicity tests are available to represent the category for these endpoints.

Algae. EPA disagrees with the submitter that the algal tests were conducted according to OECD, EPA, or ASTM test guidelines for this endpoint, and considers the two submitted algal studies inadequate and of limited value. A 72- or 96-hour test duration for algae is required before a determination of data adequacy can be rendered.

Specific Comments on the Robust Summaries

Health Effects

Of twelve of health effects robust summaries, none gave the full chemical name of the test material.

Reproductive toxicity. A robust summary for a two-generation gavage assay in rats for PNA provided sufficient information to evaluate the study methods, but was missing details about the results that would be needed to verify the study NOAEL and the overall study adequacy (which depends upon the administration of an effective dose).

Developmental toxicity. The summary for the study on ONA provided sufficient information to verify the validity of study methods, but did not provide sufficient information on maternal toxicity (especially clinical signs) to verify the assignment of the NOAEL; the summary assigned a higher NOAEL than Table 9 of the test plan, but it is possible that both are incorrect, and that the lowest dose was the NOAEL. Providing data from a pilot range-finding study could help support this study.

Ecological Effects

Algae. Water hardness is the only missing data element for ONA, and needs to be submitted if available.

Followup Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

References

Chemicals inspection and Testing Institute; Biodegradation and Bioaccumulation Data of Existing Chemicals Based on the CSCL Japan; Japan Chemical Industry Ecology-Toxicology and Information Center, ISBN 4-89074-101-1 p. 3-42 (1992)

Alexander, M. and Lustigman, B.K. Effect of chemical structure on microbial degradation of substituted benzenes. J. Agric. Food Chem. 14:410-413 (1966)